

Applicant: Ridwan Shabsigh
Serial No.: 10/658,991
Filed: September 9, 2003
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REMARKS

Claims 9, 10, 13-15, 17-19 and 21 were pending in the subject application. Applicant has herein amended claims 9 and 18 and canceled claims 14, 15 and 17. Upon entry of this Amendment, claims 9, 10, 13, 18, 19 and 21 will be pending.

Support for the amendments to claims 9 and 18 may be found, inter alia, on page 28, lines 9-12 and on page 28, lines 31-35.

Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 9, 10, 13-15, 17-19 and 21 under 35 U.S.C. 103(a) as allegedly unpatentable over U.S. Patent No. 5,652,225 (Isner) and U.S. Patent No. 6,100,286 (Lowrey) in view of Christ, GJ., (1995) Urology Clinics of North America, 22(4): 727-45. The Examiner asserted that Isner disclosed injecting VEGF-encoding nucleic acids for inducing angiogenesis and taught plasmids encoding VEGF164/165 (the Examiner referred to FIGURE 5 (b) and EXAMPLE 2 of Isner). The Examiner also asserted that Lowrey disclosed that one organ which suffers from vascular insufficiency is the penis (the Examiner referred to TITLE, BACKGROUND OF INVENTION of Lowrey). The Examiner additionally asserted that Lowrey cited several patents to demonstrate that one such tissue is the corpora cavernosa (*Id.*). The Examiner asserted further that it was known at the time of invention that a very common mechanism of erectile dysfunction was vascular insufficiency (Christ, GJ., cited in page 1 of the specification).

The Examiner then asserted that at the time of invention it

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would have been obvious to treat a subject suffering vascular insufficiency of the penis because one of the deficiencies of erectile dysfunction is due to insufficient blood flow. The Examiner also asserted that treatment could be accomplished by injection into the corporal tissue with plasmids encoding VEGF164/165 since the Artisan would do so to treat the disease by increasing vascularization. The Examiner additionally asserted that the Artisan would have a reasonable expectation of success, as Isner discloses that upon delivery of VEGF, increased angiogenesis would occur.

Applicant's response

In response, applicant respectfully traverses the Examiner's rejection. Applicant maintains that it would not have been obvious to treat a subject suffering vasculogenic erectile dysfunction of the penis based on the Examiner's cited prior art.

Applicant notes that Isner et al. discloses the use of a hydrophilic polymer incorporating a nucleic acid wherein the nucleic acid-bearing hydrophilic polymer is brought into contact with cells of an artery or blood vessel by coating a balloon-catheter to effect angiogenesis (see claim 1 of Isner et al.). However, Isner et al. does not suggest treating erectile dysfunction. Lowrey specifically discloses the administration of *vasodilator* agents to the circulating blood of a subject in an amount effective to increase blood flow to the genitalia (see Lowery, column 3, lines 46-47) but does not teach or suggest that administration of agents that effect vasculogenesis would or could accomplish such result. Importantly, Lowery is silent

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with regard to increasing vascularization and angiogenesis, and does not suggest treating vasculogenic erectile dysfunction with a vasculogenic agent.

The mechanism and effect of vasodilation as disclosed by Lowery, wherein blood flow is increased by the widening of existing blood vessels, is different to the mechanism and effect of vasculogenesis effected by the expression of VEGF as claimed by applicant, which creates new vessels. The mechanism and effect of vasodilation is also different from the mechanism and effect of vasculogenesis disclosed by Isner. Thus, even if one combines Lowery with Isner, there is no suggestion of treating vasculogenic erectile dysfunction with a vasculogenic agent (which is not taught in either reference). Moreover, there is no reasonable expectation of success that a method of treatment of a specific disease with a vasodilating agent can somehow be applied to a different disease in addition to substituting the agent with a vasculogenic agent, i.e. an agent that works by a completely different mechanism.

Furthermore, Lowrey teaches that "non-invasive" methods (see column 3, lines 36-37) and "rapid" onset which Lowery achieves with vasodilator agents, are preferred (see column 3, lines 37-38). Thus, Lowery teaches away from the claimed invention which requires introducing a gene into a cell of the penis so as to cause vasculogenesis. At minimum, Lowery would lead one of ordinary skill the art to question whether a combination of a reference (Lowery) calling for a non-invasive and rapid onset method with a reference (Isner) calling for an invasive (balloon catheter) and non-rapid onset method (angiogenesis) would be expected to be successful.

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With regard to the Examiner's citation of Christ, GJ., applicant respectfully requests that the Examiner specifically cite where in Christ, GJ. there is a teaching of "vascular insufficiency". Applicant has been unable to identify such teaching. Applicant does note, however, that Christ, GJ. discloses that the etiologic basis of erectile dysfunction is related to primary changes in corporal smooth muscle physiology/function (column 2, first paragraph). As such, Christ, GJ. would not lead one of skill in the art to treat erectile dysfunction with an agent that effects vasculogenesis as recited in the amended claims. Thus the combination of Isner, Lowery and Christ does not teach or suggest the invention as claimed.

Unpredictability as referenced by the Examiner

Applicants respectfully note that at various points throughout the prosecution of this application the Examiner has indicated that the level of unpredictability in the art is high. In the April 3, 2008 Office Action the Examiner asserted that, "the Artisan would naturally find that VEGF is not reasonably predictable to treat any form of erectile dysfunction." (page 2, last line, emphasis added). Also, in the November 13, 2006 Office Action, the Examiner asserted that the prior art research in VEGF indicates that the physiology of the body is such that it is not reasonably predictable that any particular tissue could be so-treated to increase/maintain vascularization, whether other factors may be required, and at what time VEGF may be required for treatment. Furthermore, the Examiner asserted that the Artisan would necessarily immediately recognize that the simple expression of VEGF in any particular tissue would not necessarily maintain or increase blood vessels in that tissue

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(page 13, first paragraph).

In view of the Examiner's extensive admissions that the effects of VEGF were unpredictable in the art, it is an unreasonable position to now assert the contradictory position that the use of VEGF would predictably treat vasculogenic erectile dysfunction. Such is especially so considering that the primary reference used in the obviousness rejection, Isner, does not suggest treating any form of erectile dysfunction with VEGF, and where the Lowery reference discloses a different form of erectile dysfunction with a completely different class of agent which works via a different mechanism.

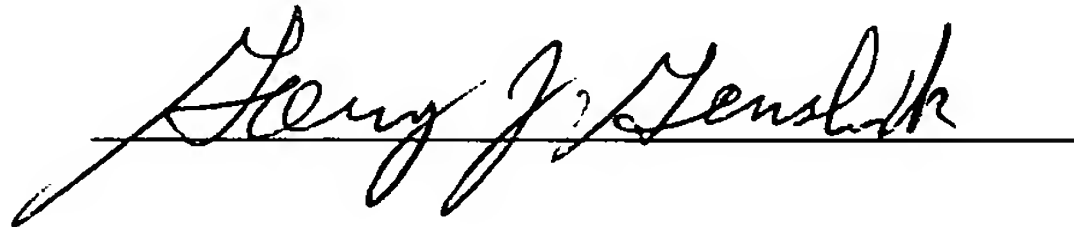
Thus, applicants maintain that Isner, Lowery and Christ in combination, do not render applicant's claimed invention obvious, nor would the Artisan have any reasonable expectation of success in view of unpredictability in the field acknowledged by the Examiner. Accordingly, applicants request the Examiner reconsider and withdraw the rejection.

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If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

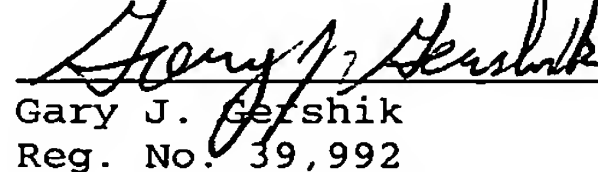
No fee, other than the enclosed \$65.00 fee for a one-month extension of time, is deemed necessary in connection with this Amendment. In the event that any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account 03-3125.

Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

 4/6/09
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